

REMARKS

The Invention

The invention features injectable polymeric compositions including a physical chemical protecting group or organic solvent and methods of their use. The polymers are capable of forming a hydrogel in situ and are useful for sustained drug delivery and to prevent postoperative adhesions.

Claim Amendments

Claims 15, 16, and 18 have been amended solely for emphasis. No new matter has been added.

The Office Action

Claims 1-21 are pending. Claims 1-14 stand rejected for obviousness over Parker et al. (U.S. Patent No. 6,218,464; hereafter "Parker) in view of Jodal et al. (Starch 1984, 36:140-143; hereafter "Jodal"). Claim 17 is rejected for obviousness over Parker in view of Jodal and Rhee et al. (U.S. Patent No. 5,324,775; hereafter "Rhee"), and Claims 15, 16, and 18-21 stand rejected for obviousness over Harmer et al. (U.S. Patent No. 6,281,400; hereafter "Harmer") in view of Rhee. These rejections are addressed below.

Rejections under 35 U.S.C. § 103(a)

Parker

Claims 1-14 stand rejected for obviousness over Parker in view of Jodal, and claim 17 stands rejected for obviousness over Parker in view of Jodal and Rhee. Applicants again note that the teachings of Jodal appear to be relevant only to claims 2, 13, 14, and 17.

The legal standard for obviousness is recited in M.P.E.P. § 2142, which states:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

This standard has not been met in the present case.

Independent claims 1, 2, 14, and 17 recite hydrogel or hydrogel precursor compositions including “a polymer comprising a water soluble polymer domain with at least two hydrophobic interacting groups attached thereto” (emphasis added). In contrast, the polymers of Parker do not contain a water soluble domain, as required by instant claims 1-14 and 17.

In reply to this argument, the Office states:

it is noted that the monomer mixture disclosed by Parker et al. comprises one monomer having high water solubility attached to one fluorinated monomer and to one non-fluorinated monomer having low water solubility (See col. 2, lines 9-15). Thus, the polymer disclosed by the patent comprises a water-soluble domain with at least two hydrophobic interacting groups, as claimed by Applicant. (emphasis added)

This statement is scientifically incorrect. The Office appears to confuse the terms “monomer” and “domain,” which are not synonymous. A polymer domain is a region of a polymer containing a plurality of monomers, i.e., a single monomer is not a domain. This point is illustrated on page 14, ll. 1-18 of the specification, which gives exemplary domains and notes the polymeric – not monomeric – nature of the domains. Thus, nowhere does Parker teach or suggest polymers having a water soluble domain, as required in the instant claims.

As stated in Applicants’ previous reply, Parker is directed to the synthesis of random copolymers of fluorinated and water-soluble monomers. Since the polymerization of Parker is random, the water soluble monomers are dispersed randomly throughout the polymer rather than in distinct domains. Furthermore, the random copolymers of Parker include less than or equal to 10% of a highly water-soluble non-fluorinated monomer, making the polymers water repellant.

In rejecting these arguments, the Office states, “Applicant’s [sic] claimed invention is directed to a polymer comprising a water-soluble polymer domain, and not to [a] water-soluble copolymer, as argued by Applicant.” Applicants,

however, never made this argument. The Office appears to be referring to Applicants' arguments about the water-repellant nature of the polymers of Parker. Regarding this water repellent nature, the Office states that "the fact that the compositions may be used to increase water repellency when applied to surfaces does not prevent said compositions from forming a hydrogel, once the cyclodextrin is removed." Again, this position is scientifically incorrect. The fact that the polymers of Parker are water repellent (col. 5, ll. 49-61) does mean that the polymers do not form a hydrogel. Hydrogels of the invention by definition require polymers that absorb, not repel, water, and it is self evident that a water repellent material will not absorb water.

Jodal does not remedy the deficiencies of Parker as it merely describes the kinetics and products of the enzymatic degradation of cyclodextrin and says nothing regarding water soluble polymer domains. In sum, neither Parker nor Jodal teach or suggest the limitations of the instant claims, and, for this reason alone, the rejection for obviousness should be withdrawn.

Regarding claims 2, 13, 14, and 17, Applicants further assert that there is no motivation to combine Parker with Jodal. In addition to Applicants' previous arguments on motivation, M.P.E.P. § 2143.01 states, "If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." As acknowledged by the Office (pg. 7), the invention of Parker is

directed to reducing or eliminating gel formation during a polymerization by employing cyclodextrin (col. 7, ll. 33-37). To provide the motivation required for obviousness, the Office relies on the assumption (with which Applicants continue to disagree) that one would be motivated to remove the cyclodextrin from the polymers of Parker to form a hydrogel. Assuming that removing the cyclodextrin would result in formation of a hydrogel (which Applicants do not concede), such a removal would achieve the opposite result desired by Parker, thus rendering the composition of Parker unsatisfactory for its intended purpose. The Office's arguments thus fail to support a motivation to combine under the guidelines required by M.P.E.P. § 2143.01, and the rejection should be withdrawn on this basis as well.

Claim 17 is directed to a method of incorporating a sensitive biological material into a hydrogel of the invention by combining the composition of claim 1 with a sensitive biological material and then employing a disrupting molecule to initiate gelation. A failure to establish a *prima facie* case of obviousness for claim 1 renders claim 17 non-obvious as well. As stated above, Parker and Jodal do not teach or suggest the limitations of claim 1, and, in addition, there is no motivation to combine the references. The Office also acknowledges that Rhee does not teach or suggest the limitations of claim 1, and, thus, the rejection of claim 17 should be withdrawn as well.

Harmer

Claims 15, 16, and 18-21 stand rejected for obviousness over Harmer in view of Rhee. Applicants again traverse this rejection.

Claims 15, 16 (from which claims 19-21 depend), and 18 recite the step:

(a) providing a solution comprising a polymer comprising a water soluble polymer domain having at least two hydrophobic interacting groups attached thereto, wherein said hydrophobic interacting groups bind strongly to each other in an interchain manner to form a hydrogel under physiological conditions, and a water soluble organic solvent, said organic solvent preventing gel formation of said polymer

Thus, each of the claims requires the provision of solution containing (i) a polymer that gels under physiological conditions by interchain binding of hydrophobic interacting groups and (ii) an organic solvent that prevents the hydrophobic interacting groups from binding to form a gel, i.e., the provision of a solution of a polymer that does not gel because of the presence of the organic solvent. To emphasize this point, the claims have now been amended to recite that gelation occurs through the strong interchain binding of the hydrophobic interacting groups once the organic solvent is removed. Nowhere does Harmer teach or suggest what is claimed.

In maintaining the rejection in view of Harmer, the Office states:

it is noted that the silicate composition disclosed by Harmer et al. is mixed with the fluorinated polymers before gelation (See col. 4, line 62 to col. 5, line 67). The comprising language of the claims in the instant application allows for additional ingredients in the compositions disclosed by the prior art. The method disclosed by

Harmer et al. includes removing the organic solvent from the polymer composition and forming a gel, as claimed by Applicant.

This statement is incorrect.

As stated in the previous reply, the fluorinated polymers disclosed by Harmer are water-soluble and do not form gels upon removal of an organic solvent, unlike the polymers of instant claims 15, 16, and 18. The teachings of Harmer support this position. For example, Harmer states:

The highly fluorinated ion-exchange polymers are used within the context of the present invention in a liquid composition form (also called a solution) which can be ... modified as needed to remove a portion of the water, alcohols or any volatile organic by-products by distillation or other methods known in the art to give a liquid composition consisting essentially of the water and the polymer. (col. 4, l. 62 – col. 5, l. 4; emphasis added)

The passage, “a liquid composition consisting essentially of the water and the polymer” clearly indicates that the fluorinated polymers of Harmer do not form a gel when an organic solvent is removed. In contrast, the instant claims require a polymer that does form a gel when an organic solvent is removed. The fluorinated polymers of Harmer have properties opposite those required by the instant claims.

The Office tries to supply teachings missing in Harmer by reference to gelation of silicate and Applicants’ use of the term “comprising.” The Office apparently assumes that any gelation is sufficient to render the instant claims obvious. It is, however, indisputable that claims 15, 16, and 18 require gelation of a polymer through strong interchain binding by two or more hydrophobic interacting groups, and the claims have been amended to emphasize this point.

The silicate gelation of Harmer does not meet this limitation. Harmer teaches that the silicate is sodium (Na^+), ammonium (NH_4^+), or potassium (K^+) silicate (an anion containing Si and O), or combinations thereof (col. 5, ll. 39-40). These silicates are inorganic compounds that do not have hydrophobic interacting groups. Thus, any gelation of silicate in Harmer cannot occur through interchain binding of hydrophobic groups, as required by the instant claims. Since neither the fluorinated polymers nor the silicates disclosed by Harmer form a gel as in claims 15, 16, and 18, Harmer does not teach or suggest each and every limitation of the instant claims, and the rejection should be withdrawn.

If the Office persists in this view, Applicants request that the Examiner point to specific language in Harmer that teaches the gelation of a polymer by strong interchain binding between hydrophobic interacting groups.

As noted by the Office, Rhee is only cited for the prospect of teaching gelation in contact with tissues and does not remedy the deficiencies of Harmer.

Based on the foregoing reasons, the rejection of claims 1-14 over Parker and Jodal, the rejection of claim 17 over Parker, Jodal, and Rhee, and the rejection of claims 15, 16, and 18-21 over Harmer and Rhee should be withdrawn.

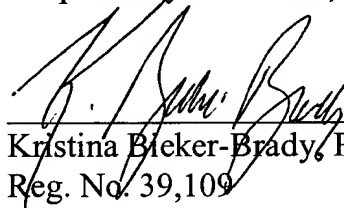
CONCLUSION

Applicants submit that the claims are now in condition for allowance, and such action is respectfully requested. If the Office does not believe the claims are allowable, Applicants request that the Examiner contact the undersigned to schedule an interview with the Examiner and her supervisor.

Enclosed is a petition to extend the period for replying for three months, to and including March 26, 2004. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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